B2 The universal array of the invention may be synthesized in 5'-3' direction (FIGURE 1) and 3'-5' direction (FIGURE 2). U.S. Patent Number 6,310,189 which is incorporated herein by reference for all purposes, disclosed specific methods for synthesizing oligonucleotide probes on a substrate in 5'-3' direction.

IN CLAIMS

Please amend Claims 1 & 4:

B3 SUB C1

1. A method for detecting a plurality of nucleic acid targets in a sample comprising:

hybridizing the sample with different mediator nucleic acids and at least 50 different cipher probes immobilized on a substrate, wherein each of the mediator nucleic acids has a first subsequence that is complementary with one of the nucleic acid targets and a second subsequence that is complementary with one of the cipher probes; and
detecting at least 50 different nucleic acid targets in the sample based upon the hybridization pattern.

B4 SUB C1

4. (amended) The method of claim 3, wherein the cipher probes do not substantially hybridize with any nucleic acid in the sample.

REMARKS

Applicants wish to thank the Examiner for the courtesy extended during an interview between the Examiner and the Applicants' attorneys.

Applicants have amended claims 1 and 4. Support for the amendment for claim 1 is found throughout the application and is particularly found at page 38, lines 14-18, and page 29, lines 2-7. Support for the amendment for claim 4 is found throughout the application and is particularly found at page 4, lines 4-7.

Applicants respectfully request reconsideration of the pending rejection and reexamination of the present claims in light of the amendments and the remarks detailed below. It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled.

Specification

The examiner has objected to the specification because specification lists attorney docket numbers. Applicants have replaced the attorney docket numbers with application numbers in the specification.

Applicants have also amended the specification to update the status of US applications referenced in application.

Obviousness Rejection Under 35 U.S.C. §103(a)

Claims 1-16, 18 & 20-24 are rejected under 35 USC 103(a) as allegedly being unpatentable over Urdea et al. (1989) in view of Lockhart et al. (2000). Applicants respectfully disagree with the Examiner. However, for the purpose of expediting the issuance of claims, Applicants have amended Claim 1 to recite "at least 50 different nucleic acid targets," etc.

Urdea et al discusses methods for detecting a single analyte using a binding probe (B, figure 1) and a label probe (A, figure 1). A target is bound by multiple probes in multiple regions (Figure 1). No methods for detecting multiple analytes are disclosed. As pointed out by the Examiner, no hybridization pattern is generated for detection. In contrast, Claims 1-16, 18 & 20-24 recite methods for detecting a plurality of at least 50 targets and including a step of "detecting the nucleic acid targets based upon the hybridization pattern."

The Office Action alleges that one of skill in the art would be motivated to combine Urdea et al. with Lockhart et al. in order to detect multiplicity of genes in order to provide a high throughput analysis of multiple genes with high signal to noise ratio.

Applicants respectfully submit that the discussion by Urdea et al does not provide any motivation or suggestions to use multiple probes in microarray assays. One primary advantage of the Claimed methods is the flexibility of the assay, i.e., one type of array

can be used as a universal array to detect different sets of targets by using different mediator probes, in contrast, Urdea et al.'s motivation was to increase sensitivity.

Because there is no motivation or suggestion in the cited references to combine the cited references, applicants respectfully submit that the Examiner has failed to establish a prima facie obviousness. Therefore, this rejection of Claims 1-6, 18 and 20-24 should be withdrawn.

Claims 17 and 19 are rejected under 35 USC 103(a) as allegedly being unpatentable over Urdea et al. in view of Lockhart et al and further in view of Vinayak et al. For the above reasons, applicants respectfully submit that it is not prima facie obvious to use mediator and cipher probes to detect multiple analytes. Therefore, this rejection of Claims 17 and 19 should also be withdrawn.

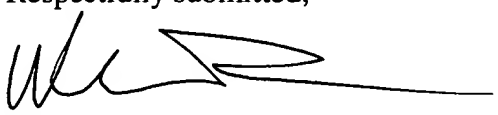
CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5699.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE APPLICATION

In the Specification

Please amend the following paragraph on page 38, lines 1-7:

The fluorescence intensity data (or other signals) detected may be processed as described for gene expression monitoring without extension reaction. Some of the data processing methods are described in, *e.g.*, U.S. Patent Nos. 6,040,138 and 5,800,992, U.S. Patent Application Serial Numbers 09/528,414, [_____, attorney docket number 3357.1, _____, attorney docket number 3298.1, _____, attorney docket number 3309, _____, attorney docket number 3364, and _____, attorney docket number 3369.1,] all incorporated herein in their entireties by reference for all purposes.

Please amend the following paragraph on page 30, lines 13-16:

The universal array of the invention may be synthesized in 5'-3' direction (FIGURE 1) and 3'-5' direction (FIGURE 2). [U.S. Patent Application Serial Number 09/490,580,] U.S. Patent Number 6,310,189 which is incorporated herein by reference for all purposes, disclosed specific methods for synthesizing oligonucleotide probes on a substrate in 5'-3' direction.

In the Claims

Please amend Claims 1 & 4 as follows:

1. (amended) A method for detecting a plurality of nucleic acid targets in a sample comprising:

   hybridizing the sample with [a plurality of mediator] different nucleic acids and [a plurality of] at 50 different cipher probes immobilized on a substrate, wherein each of the mediator nucleic acids has a first subsequence that is complementary with one of the nucleic acid targets and a second subsequence that is complementary with one of the cipher probes; and

   detecting at least 50 different [the] nucleic acid targets based upon the hybridization pattern.

4. (amended) The method of claim [4] 3, wherein the cipher probes do not substantially hybridize with any nucleic acid in the sample.